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# Bioinformatic Analysis of Selected Natural Compounds for Antidiabetic Potential

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**ABSTRACT**

Diabetes is a very serious, chronic, and complex metabolic disorder that is based on multiples aetiologies with both acute and chronic. There are two types of diabetes, one types 1 DM and the other is type two DM. Both T1DM and T2DM are the most serious type of chronic conditions that are typical cannot be cured. Insulin stimulates adipocytes, myocytes, and hepatocytes, which uptake glucose from the circulatory system. Antidiabetic drugs show useful effects through decreasing glucose absorption in the intestines increasing insulin levels in the body or increasing the body's sensitivity (or decreasing its resistance) to insulin. Most of these plants contain bioactive compounds. Such compounds are alkaloids, flavonoids, glycosides, terpenoids, carotenoids, etc., which are frequently implicated as having an Antidiabetic effect. The different types of phytochemicals include flavonoids, saponins, phenolic acids, alkaloids, tannin, stillness, and polysaccharides.

They have two types of drug design: structure-based drug desing& ligand-based drug design. The protein is a structure-based- ligand, which is based on drug design for the role of significantly quantitative structure-activity relationship (QSAR) & pharmacophore analysis. Ligand-based pharmacophore model generation depends on the information regarding the known biological activity without any structural information depends on the macromolecular target. The ligand-based VS is more expensive due to structure-based methods. Based on the opposing chemical functionalities, and the geometric arrangement about each other, where the interactions are observed there is the pharmacophore features are placed on the ligand side.

***KEYWORDS**: Diabetes, Anti-diabetes, T1DM, T2DM, drug design, ligands, Insulin etc*

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## INTRODUCTION

Diabetes is a very serious, chronic, and complex metabolic disorder that is based on multiple aetiologies with both acute and chronic symptoms [Soumya et al., 2011]. About 25% of the population is estimated about 25% is affected by this disease [Arumugam and Manjula et al., 2013]. The genetic environmental factors are contributing to the development of diabetes [Murea and Freedman et at., 2012]. Type-2 diabetes is a chronic metabolic impairment that affects the quality of life. Currently, they cause of death with 1.5 million deaths from type-2 diabetes. Type-2 diabetes causes blood glucose and cannot produce enough insulin in the body, which is also known as insulin resistance in insulin-targeting tissues such as adipocytes, liver, skeletal muscle. The body's insulin resistance causes glucose to remain in the blood. The insulin is released by the pancreatic β-cells which is the hormone responsible for glucose homeostasis [Grisham et at., 1997]. Insulin stimulates adipocytes, myocytes, and hepatocytes, which uptake glucose from the circulatory system [Berg and Stryer et al., 2002]. For example, plants have been used to prevent conditions associated with diabetes [Soumyanath etal., 2006].

However, damaging the other organs owing to the high level of sugar, which leads to loss of cardiovascular diseases, vision, and Kidney failure. Chronic hyperglycemic determine diabetes with the interference in the macromolecules metabolism, the impairments in insulin secretion, or insulin action established the result [Somaya et al., 2011]. Diabetes causes, dysfunction, long-term damage, and failure of various organ systems (heart, blood vessels, eyes, kidneys, and nerves), which cause disability and premature death [Salsali et al., 2006]. Several symptoms such as blurring of vision, thirst, polyuria, and weight loss also show diabetes [Weinzimer and Phillip et al., 2014].

## TYPES OF DIABETES MELLITUS

There are two types of diabetes, one types 1 DM and the other is type 2 DM. T1DM is a chronic condition in which the pancreas produces little or no insulin, it is well known as insulin-dependent diabetes or juvenile diabetes. [Assail and

Nathan et al., 2006]. Those patients who suffer from type 1 DM need to control the amount of glucose in their blood and they are prone to ketoacidosis. Mostly the T1DM takes place in adolescents and children [Folorunso et al.,2013]. On the other hand, T2DM is also called non-insulin-dependent diabetes, and its results depend on the body's ineffective use of insulin and hyperglycemia [Spellman and Chavez et al., 2010]. Around the world so many people are diabetic. Impaired of the body to insulin is based on reducing the quality of target tissue with the circulating level of insulin is normal [Chavez etal., 2010].

Ethnicity, family history of diabetes, and smoking increase diabetes risk, older age, unhealthy diet, overweight and obesity, physical inactivity, and previous gestational diabetes [Oguntibeju et al., 2013]. In their project the WHO ask the seventh leading cause of death in 2030 due to diabetes [ Kakkar et al., 2016]. The number of patients with diabetes older than 64 years the number will be as compared to that in developed countries (≥48million) are greater in developing countries(≥82). The project increases and occurs in the Middle East crescent, sub- Saharan Africa, and India [Narayan and Williams etal., 2006].

**TARGETING TYPE 2 DIABETES**

Both T1DM and T2DM are the most serious type of chronic conditions that typically cannot be cured. However, all forms of diabetes have been treatable due to the development of readily available insulin since 1921. The enhancement of insulin secretion by pancreatic islet βcells is a treatment of T2DM. Antidiabetic drugs or hypoglycemic agent medications work based on lower blood glucose concentrations (i.e., the amount of sugar in the blood). There are different classes of antidiabetic drugs, which depend on the natural selection of diabetes and their age and situation of the person, as well as other factors. Antidiabetic drugs show useful effects through (Soumya et al., 2011) decreasing glucose absorption in the intestines (Murea and Freedman etal., 2012) increasing insulin levels in the body, or (Arumugam and Manjula et al., 2013) increasing the body's sensitivity (or decreasing its resistance) to insulin [Chen et al., 2007].

The treatments are considered to be unsatisfactory because of the prevention of complications and preservation of quality of life. The α-glucosidase inhibitors, like acarbose and miglitol, while effective at decreasing the absorption of glucose due to interfering with the action of α-glucosidases which is present in the small intestinal brush border. It is associated with abdominal bloating, diarrhea, and flatulence. Conventional insulin secretagogues, such as sulfonylureas and the class of meglitinides, both showed their result in the induction of hypoglycemia. Metformin is the first-line drug treatment of T2DM, which is particularly in overweight and obese patients and those with normal kidney function [Burns et al., 2007]. Agonists of the peroxisome proliferator-activated nuclear receptor (PPAR), thiazolidinediones, are capable of reducing insulin resistance and safety concerns. The use of rosiglitazone has been severely restricted in the US, which has been completely suspended in Europe due to concerns about its cardiovascular safety [Mohr et al., 2010].

**ROLE OF ANTIDIABETIC DRUGS IN DIABETES**

Antidiabetic drugs are all pharmacological agents except insulin which has been approved for hyperglycemia treatment in type two diabetes mellitus (DM). These drugs are classified according to their fundamental mechanism of action as insulinotropic or non-insulinotropic. Oral hypoglycemic drugs have different types of classes that exert antidiabetic effects by different mechanisms, like as biguanides, thiazolidinediones, non-sulfonylureas secretagogues, sulfonylureas, and α-glucosidase inhibitors. To reduce the level of sugar in the blood of oral sulfonylureas, namely glimepiride and glyburide, mainly by elevating insulin release from islets of Langerhans [DeFronzo and Inzucchi et al., 1999]. Traditionally, Gynura species are widely studied for their anti-diabetic properties, specifically, Gynura procumbens [Atangwho et al., 2013]. Instant, due to lowering blood glucose levels they possess other beneficial physiochemical properties such as antihypertensive, anti-inflammatory, chemo preventative actions, and antiulcerogenic [Lee and Li et al., 2015].

However, studies on G. bicolor are not as extensive as procumbens, but it is reported to have high antihyperglycemic properties because of the presence of flavonoid compounds such as caffeoylquinic acid and caffeic acid groups [Abdul and Zhou et al., 2016]. Plant natural products, diabetes mellitus, mechanistic studies, insulin, , therapeutic targets, chemical scaffolds, artemisinin, lovastatin, semi-synthetic derivatives, natural products, drug-like properties ,glucose absorption, lipid metabolism, Anti-Diabetic, inhibitor acarbose, glargine, a-glucosidase, herbal medicines, biguanides, b-cell proliferation, drug-like diversity, in-silico drug discovery, autoimmune disease, Glibenclamide, Mitiglinide, Orlistat, Rosiglitazone, Aleglitazar, Miglitol, Nateglinide, Repaglinide, Tolbutamide, Berberine, Ginsenoside Rg3 ,cardiovascular diseases, hyperglycaemia, peroxisome proliferator-activated receptor (PPAR), , CH10 from *Momordicacharantia*, Isoflavin C, *Isotanshinone*, *Psoraldin*, Sanggenon C, GSK3, *Salacia reticulata*, a-glucosidase inhibitor *Acarbose* ,insulin action, voltage-sensitive Ca2+ channels, b-cells, insulin-releasing properties, MIN6 cells, AMP kinase, *Acarbose* , Nymphayol, Oleanolic acid, Resveratrol, Sulphostin, GLP1-like, plasma enzyme dipeptidyl peptidase IV (DPP IV), Abyssinone-VI-4-O-methyl ether, Apigenin fucopyranoside, *Bakuchiol* ,*Piper longum*.

**MEDICINAL PLANTS SOURCE USED IN ANTIDIABETIC AGENTS**

The plant extract is a natural product that is not causing harm for patients and plants play a vital role in the development of the drug in upcoming years. [Morais and Setzer et al., 2018]. So many plants are providing those sources of bioactive chemicals, which are not causing side effects and the plants have so many powerful pharmacological actions [Roberts et al., 2018]. For centuries, many types of plants are considered as a fundamental source of potent antidiabetic drugs [Arumugam and Manjula et al., 2013]. Nowadays, to treat the disease diabetes using those medicine which is made by plants those possess antidiabetic activities and contain various phytoconstituents. Such phytoconstituents are flavonoids, glycosides, terpenoids, saponins, alkaloids, and carotenoids [Roberts et al., 2018]. Also study marked by Durazzo et al. [Camilli et al., 2018], that shows the combined action of different biologically active compounds (i.e., polyphenols, lignans, glucosinolates, carotenoids, coumarins, etc.) which leads to the potential beneficial properties for Antidiabetic drugs.

Generally, certain types of approaches are study [Durazzo et al., 2017] due to interactions of phytochemicals can be classified: (i) study the model system development of

interactions [Heo et al., 2007 and tabard etal., 2009]; (ii) characterization of biologically active compound-rich extracts [Rugina et al., 2015] or (iii) study of extractable and non-extractable compounds [Calixto et al., 2012]. The medicinal plants provide benefits in the hypoglycemic properties for the management of diabetics. It describes medicinal plants (i.e., *coffee, nettle, banana, sage, soybean, bitter melon, aloe, cinnamon, fenugreek, guava, cocoa, green and black tea walnut, turmeric, and yerba mate*) used in the treatment of diabetes and natural product of plant have the mechanism to treat diabetes as antidiabetic agents, a compound which used to treat have a high interest such as phlorizin, fukugetin, trigonelline, honokiol, amorfrutins, gymnemic acids, berberine and palmatine [ Rios et al., 2012].

**ANTIDIABETIC SUBSTANCESFROMMEDICINAL PLANTS**

So many plants are used in the treatment of diabetes, only those plant species are being used which have hypoglycemic activity and also contain bioactive compounds. Compounds having antidiabetic potential are terpenoids, flavonoids, alkaloids, and glycosides. Some plants which are used in the treatment are given below:

**ACACIA ARABICA (FABACEAE)**

*Acaciaarabica*is also known as Babool. It is used in the treatment of diabetes. Babool has the mechanism to treat this disease. It is used in traditional medicine in India to treat diabetes Mellitus. From Acacia Arabica two doses of chloroform extracts were evaluated in alloxan-induced diabetic albino rats [Patil et al., 2011]. In the test of chloroform extract of *Acaciaarabica* two types of doses were tested which are showed their antidiabetic effect. It decreases the level of serum glucose and restoring TC, TG, the level of high-density lipoprotein (HDL), and low-density lipoprotein (LDL). In the experiment scientist studied that it plays a vital role, extract of *Acacia arabica* and streptozotocin-induce diabetic rats play a vital role in the decrease in serum glucose, TG, LDL, TC level and play a vital role in increase the level of coenzyme Q10 in a dose-dependent manner and HDL and decrease the level of malondialdehyde (MDA) [Hegazy et al., 2013].

**ACHYRANTHES RUBROFUSCA (AMARANTHACEAE)**

*Achyranthes rubrofusca* which belongs to the family of Amaranthaceae is also known as 'Kadaladi'. The leaves of the *Achyranthes rubrofusca* are used to make traditional medicine. The aqueous and ethanolic leaves extract of *Achyranthes rubrofusca* are studied to show their hypoglycemic activity in alloxan-induced diabetic rats [Geetha and Sankar et al., 2011]. Decrease the level of blood glucose by these two extracts (200mg/kg, p.o. for 28 days), and this extract is increased their pancreatic enzyme, also decrease the levels of superoxide dismutase (SOD), catalase, and glutathione.

**ALBIZZIA LEBBECK (FABACEAE)**

*Albizzia lebbeck* is from the family of leguminous it is commonly known as Shirisha. In the treatment of diabetes, methanol/dichloromethane extract of *Albizzia lebbeck* is used. In the evaluation of streptozotocin-induced diabetic rats evaluate stem bark (400mg/k, for 30 days) from the *Albizzialebbeck* [ Ahmed et al., 2014]. When diabetic patients are treated by the *Albizzia lebbeck* decrease their glycated hemoglobin and increase the level of plasma insulin. It also decreases the level of LDL, VLDL, TC, and TG. It can observe based on the increase in CAT, glutathione, and SOD and kidney decrease the level of lipid peroxidation and liver of streptozotocin-induced diabetic rats. The histopathological analysis of this treatment is showed that it protects the organs in diabetic rats such as the liver, kidney, pancreas, and heart and reduces the lesions in a dose-dependent manner [Parikh and Gandhi et al., 2015].

**ALOE VERA (ASPHODELACEAE)**

*Aloe vera* belongs to the family of Asphodelaceae. *Aloevera* helps in reducing the sugar level and goes down at the normal state. For treatment of diabetes, *Aloe vera* extract examines in mouse embryonic NIH/3T3 cells and streptozotocin-induced diabetic mice. In observation, we observe that for four weeks the extract at a dosage of 130mg/kg per day will significantly reduce the level of blood glucose, an effect of metformin, TG, TC, and LDL. Aloe Vera stimulates the secretion of insulin and it also lows sugar levels at a normal state. I was observed that up-regulated GLUT-4 mRNA synthesis in NIH/3T3 cells in the study of the lyophilized aqueous extract of *Aloe Vera.* To show the antidiabetic effects of *Aloe vera* extract for use in the treatment of diabetes do various studies[Gunasekaran and Noor et al., 2017].

**AMARANTHUS TRICOLOR (AMARANTHACEAE)**

*Amaranthus tricolor* is also known as Tambdi bhaji or all saag and the family is Amaranthaceae. One hour before the oral tolerance test of methanolic extract of *Amaranthus tricolor* administrate different types of doses. All types of doses are loaded in mice to show antihyperglycemic activity. In the observation of this dosage test, we observe the maximum effect in decreasing glucose level by the dosage.

**ANACARDIUM OCCIDENTALE (ANACARDIACEAE)**

*Anacardium occidentale*(Anacardiaceae) is commonly known as Cashew. Reduce the blood glucose level plays a vital role. Extract load in the streptozotocin-induced diabetic rat and observe hypoglycemic activity [Sokeng et al., 1998]. Before injecting the streptozotocin injection the aqueous extracts in rats were treated twice daily or 2 days of beginning. The blood glucose level significantly low by pretreatment, compared to this the blood glucose level control in the diabetic rat after 3 days. The experiment was ended after 30 days and faster the lowering rate of blood glucose. The blood glucose levels of streptozotocin-induced diabetic rats decrease because of treatment to prevention of body weight loss, polydipsia, and polyphagia [Vaidya et al., 2017].

**AZADIRACHTA INDICA (MELIACEAE)**

*Azadirachta indica* is commonly known as NEEM and from the family of Meliaceae. A dose (200 mg/kg) of an ethanol extract from the leaves of *Azadirachta indica*(Neem) causes a hypoglycemic effect 72 h after administration with a persistence of up to 24h.

**BARLERIA PRIONITIS (ACANTHACEAE)**

*Barleria prionitis*(Acanthaceae) called Sahachara in Ayurveda. In alloxan-induced diabetic rats tested the antidiabetic activity of alcoholic extracts of root and leaves of *Barleriaprionitis* [Dheer et al., 2010]. The extract of *Barleria priorities* were reduce the level of blood glucose and glycosylated hemoglobin and increase the levels of liver glycogen and serum insulin but the antidiabetic activity of *Barleria* are non-significant.

**BAUHINIA THONINGII (FABACEAE)**

*Bauhinia thoningii* is commonly known as camel's foot tree, monkey biscuit tree, etc. The antidiabetic effects of aqueous leaf extract are from *Bauhinia thoningii* were studied in

alloxan-induced diabetic rats [Ojezele et al., 2011]. The dose (500 mg/kg) of extract for seven days in rats shows the result of the reduction in blood glucose, coronary risk index, and LDL.

**CASEARIA ESCULENTA (FLACOUTIACEAE)**

*Casearia esculenta* is commonly known as Saptrangi and from the family of Flacourtiaceae. Roots of *Casearia esculenta* are used for the treatment of diabetes. The dose (200 and 300 mg/kg, p.o.) of the extract from the *Cesaria esculenta* were restored the glucose level, urea, uric acid, albumin, and creatine level and also restored the level of the activities of diagnostic marker enzymes AST, ALT, γ-glutamyltranspeptidase (GGT) and alkaline phosphatase (ALP) [Prakasam et al., 2004].

**CATHARANTHUS ROSEUS (APOCYNACEAE)**

*Catharanthus roeusis* commonly known as Periwinkle, it belongs to the family of Apocynaceae. The blood glucose levels of hepatic enzyme activities of glycogen are reduced by dichloromethane-methanol extract of the leaves of *Canthranthus roeus* and also reduce the level of glucose 6-phosphate-dehydrogenase, malate dehydrogenase, and succinate dehydrogenase [Shyam et al., 2001]. For transport, the glucose in liver ethanolic extracts of *Catharanthus roeus*(100 and 200 mg/kg) are used for 4 weeks [Al-Shaqha et al., 2015].

**EUCALYPTUS CITRIODORA (MYRTACEAE)**

*Eucalyptus citriodora* is commonly known as lemon-scented gum. Its family is Myrtaceae. Leaves of the *Eucalyptus* are used in the treatment of diabetes, it helps to reduce the level of blood glucose.

*Eucalyptus citriodora* leaf in are extract due to alloxan-induced diabetic rats (250 and 500 mg/kg, p.o. for 21 days) [Arjun et al., 2009].

**GYMNEMA SYLVESTRE(APOCYNACEAE)**

*Gymnema sylvestre* commonly known as Australian cowplant , belongs to the family of Apocynaceae. By the in vitro and in vivo technique determined the ethanolic extract (100mg/kg, p.o. for 4 weeks) of *Gymnemasylvestre* . Observation showed that an improvement in diabetic rat and antihyperglycemic activity.

**HELICTERES ISORA (STERCULIACEAE)**

*Helicteres isora* is commonly known as the Indian screw tree and belongs to the family of Sterculiaceae. In investigation investigate the aqueous ethanol and butanol extracts of *Helicteres isora* roots (250mg/kg, p.o. for 10 days ) due to in alloxan-induced diabetic rats [Venkatesh and Madhava et al., 2010]. This process also restored the size in normal of the pancreatic islets, liver, and kidney glomeruli.

**TRIGONELLA FOENUM-GRAECUM (FABACEAE)**

The common name of *Trigonella foenum-graecum* is Fenugreek and it belongs to the family of Fabaceae. In the observation of this treatment by ethanol extracts of *Trigonellafoenum* seeds are alloxan-induced in diabetic rats gives different doses (0.1, 0.5, 1, and 2g/kg) are showing the antidiabetic effects [Ahmed et al., 2009]. The seeds of the *Trigonella foenum-graecum* were attenuated markers of inflammation and it improves the oxidative stress of endocrine function in alloxan –induced diabetic rats.

**VERNONIA AMYGDALINA (ASTERACEAE)**

*Vernonia amygdalina* is a member of the daisy family. It is a small shrub that grows in tropical Africa. Its common name in English is Bitter Leaf due to its bitter taste. There are

different combinations of metformin (50 mg/kg) antidiabetic activity and aqueous extracts of Vernonia amygdalina leaves (100 mg/kg) in normoglycemic and alloxan-induced diabetic rats [Michael etal., 2010]. They caused more reduction in *glycemia* which showed that the combinations of extract and metformin. Cold concoctions of this plant are also used in the treatment of malaria, intestinal parasites, diarrhea, and stomach upset.

**WITHERINGIA SOLANACEA (SOLANACEAE)**

*Witheringia solanacea* is a genus of flowering plants in the family of *solanaceae*, with a neotropical distribution. It is closely related to Physalis. Normal rats were treated from leaves of *Witheringiasolanaceae* at 250, 500, and 1000 mg/kg doses, and have two doses significantly which decreased blood glucose levels after 1h of a GTT [Herrera et al., 2011]. At 4h and 5h of treatment, it is observed that blood glucose levels in alloxan-induced hyperglycemic rats get reduced.

**ZIZYPHUS MAURITIANA (RHAMNACEAE)**

*Ziziphus mauritania*which is also known as Indian jujube, Indian plum Chinese date is a tropical fruit tree species belonging to the family Rhamnaceae. Petroleum ether and its aqueous extracts (200 and 400 mg/kg, p.o. for seven days) are significantly restored elevated biochemical parameters such as glucose, urea, creatinine, TC, TG, HDL, LDL, hemoglobin, and glycosylated hemoglobin [Joshi et al., 2009].

**PHYTOCHEMICALS WITH ANTIDIABETIC POTENTIAL**

The new natural antidiabetic to minimal efficacy and safety concerns current antidiabetic drugs for the hundreds of millions of individuals. This is an investigation of phytochemicals that are responsible for antidiabetic effects has been for the last few decades [Manchan et al., 2016]. The single-component of plant extracts has to attribute their mixture of phytochemicals due to the antidiabetic effect of plant materials. The different types of phytochemicals include flavonoids, saponins, phenolic acids, alkaloids, tannin, stillness, and polysaccharides. The phytochemicals have a beneficial effect based on their metabolisms such as regulation of glucose and lipid metabolism, insulin secretion, stimulating β cells, NF-kB signaling pathway which inhibition of gluconeogenic enzymes, and reactive oxygen species (ROS) protective action [Manchan et al., 2016].

**ALKALOIDS**

The following alkaloids- lupanine neferin, boldine, berberine, oxymatrine, piperine, and sanguinarine- are used for their antidiabetic activity [Christodoulou et al., 2019]. The antidiabetic impact of certain alkaloids, with special reference of molecular targets throughout the insulin-signaling pathway: the effects of berberine, trigonelline, piperine, vindoneline, evodiamine, oxymatrine and nefrine on insulin-signaling and related cascades in β cells, myocytes, adipocytes, hepatocytes and other cells; are supported with in vitro and in vivo evidence. Berberine is an isoquinoline alkaloid that is isolated from medicinal plants of *Berberis* (Berberidaceae) and has antihyperglycaemic activity due to decreasing absorption of glucose [Huang and Zhao et al., 2003]. It is to inhibit α-glucosidase and to decrease glucose transport through the intestinal epithelium [Mohan et al., 2014]. The management of T2DM and cardiovascular disease has the potential due to antioxidant,

anti-inflammatory, glucose-lowering, lipid-lowering properties [Cicero et al., 2016].

**FLAVONOIDS**

Flavonoids represent a big class of plant secondary metabolites and are shown in a high range of vegetables, herbs, and fruits. The presence of aromatic rings and hydroxyl groups in the flavonoid structure and it can play as natural antioxidants. In antidiabetic diets, flavonoids-containing products are used. So many flavonoids are namely chrysin, diosmin, catechins, kaempferol, luteolin, naringenin, quercetin, rutin, morin, silymarin, etc. In the current work of the two scientists Dens Hartogh and Tsiani, [Den et al., 2019] so, in the study of antidiabetic effects of naringenin in *in vitro* and *in vivo*. A wide variety of plants is present in fisetin. It decreases the level of blood glucose and increases the levels of glyoxalase 1 [Mackenzie and Prasath et al., 2014].

**TRITERPENOIDS**

Some plants are *Panax ginseng, Panax quinquefolium, Astragalus membranaceus, Momordica charantia, Ganoderma lucidum* and plants there present tetracyclic tripenoids [Hamid et al., 2015]. The multiple biological activities on glucose absorption; diabetic vascular dysfunction;glucose uptake; insulin secretion and retinopathy and nephropathy of oleanolic acid, glycyrrhizin, ursolic acid, lupeol, and glycyrrhetinic acid [Han et al., 2016 and Kim et al., 2013].

**DITERPENOIDS**

Triptolide is a diterpenoid that has three epoxide groups, it is isolated from *Tripterygium wilfordii.* Triptolide can decrease the levels of protein kinase B and phosphorylated inhibitor of kappaB and increased caspases 3, 8, and 9. The treatment of Triptolide is accompanied by alleviated glomerular hypertrophy and podocyte injury [Huang et al., 2013 and Gao et al., 2010].

**POLYSACCHARIDES**

The tubers of *Amorphophalluskonjac* and seed of *Cyamopsis tetragonolobus* isolated from Galactomannan polysaccharide. The rate of glucose absorption helps to decrease postprandial hyperglycemia. Helianthus tuberosus tuber contains 75 to 80% insulin in carbohydrates. The development of natural intestinal microflora after dysbacteriosis and which act as in the modulation of blood metabolism and liver enzymes [Jenkinsand and Zhang et al., 2011].

**MISCELLANEOUS**

It the improves health and survival of mice on a high-calorie diet due to resveratrol [1007]. The plasma membrane in L6 myocytes and suppresses blood glucose levels in T2DM model db/db mice is a derivative of promotes glucose uptake through glucose transporter into 4 translocations. Butein is a natural phenolic chalcone, isolated from many plant species, including *Toxicodendron vernicifluum, Dalbergia odorifera, Semecarpus anacardium, Cyclopia subternata and creopsis tungtoria.* Butein inhibits central NF-kB signaling and improves glucose homeostasis [Minakawa et al., 2012 and Benzler et al., 2015].

**COMPUTER-AIDED DRUG DESING METHODS IN THE DISCOVERY OF ANTIDIABETIC DRUGS**

The great significance is the discovery to optimization the methodologies of computer-aided drug design [CADD] in recent years (Lim et al., 2009). The process of pharmaceuticals to accelerate their approaches using CADD. They have to minimize the synthetic & biological testing efforts. Due to CADD scientists, it is determined in 3D structures of the target proteins due to the availability of experimentally CADD approaches [Zhang et al., 2011 and Ivanov et al., 2003]. They have two types of drug design: structure-based drug design& ligand-based drug design. The unknown structures of protein–ligand-based drug design are significantly quantitative structure-activity relationship (QSAR) & pharmacophore analysis. The known structure–based approaches can be used in molecular docking, which employs the structures of the targets to design the novel active compounds [Liu et al., 2011].

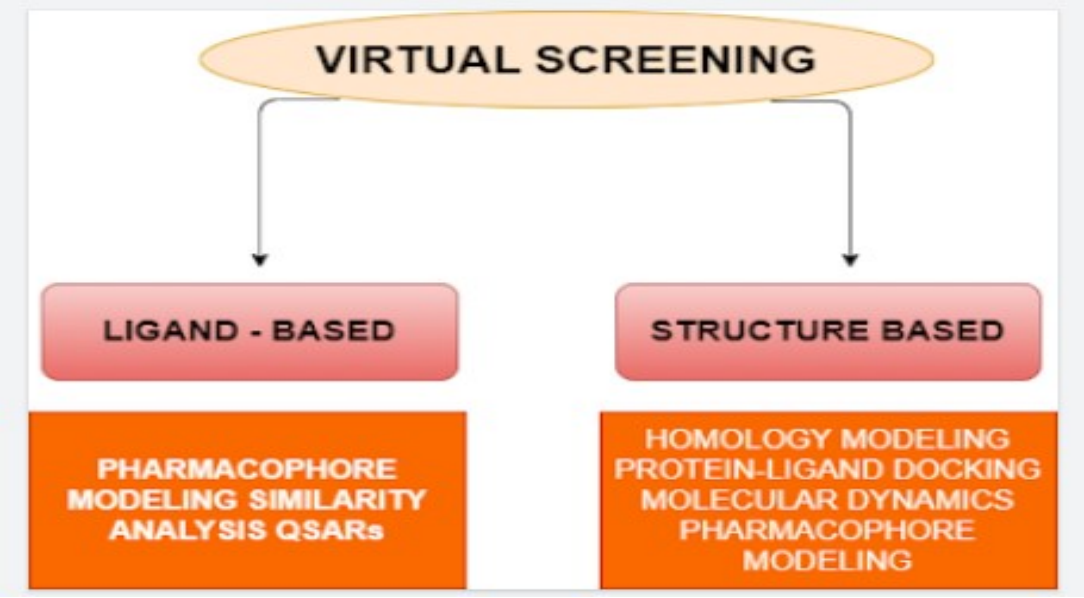
**ADMET PROPERTIES**

To apply a pharmacological effect in tissue, the blood-brain barrier, and the microcirculatory barrier, a compound has to penetrate various physiological barriers, such as the gastrointestinal barrier, to reach the blood circulation. The compound once in circulation is subsequently transported to its effector site for distribution into tissues and organs, degraded by specialized enzymes, and finally removed from the body via excretion. Such as, the distribution, absorption, excretion, metabolism, and toxicity (ADMET) properties of a compound directly affects its usefulness and safety [Song and Carter et al., 2009]. The pharmaceutical companies are trying to move ADMET evaluations into the early stages of drug discovery [Lagorce et al., 2009].

**VIRTUAL SCREENING**

Virtual screening (VS) is a computational method for identifying lead compounds from large and chemically various compound libraries. It is the computational method valuable for discovering lead, compounds in a faster, more cost-efficient, and less resource-intensive manner compared with experimental methods, such as that high-throughput screening. How to be it, the generic definition of VS was significantly wider and may encompass many different methods. VS techniques are divided into ligand-based and structure-based approaches. Scoring the method are assigns good scores to interesting molecules and worse scores to uninteresting (inactive) molecules. A successful virtual screen will provide the set of compounds for experimental screening that was highly enriched in active molecules. [Sousa etal., 2010].

The success of a particular tool VS several approaches to quantifying. Represent the enrichment factor one of the most prominent performance descriptions in VS defined the ES as (TP/n) / (A/N); where TP is the number of hits found at x % of the database, the number of compounds is n screened at x % of the database, A is the number of actives in the entire database, and N is the number of compounds in the entire database [Bayly etal., 2007 and Kirchmair et al., 2008].




**LIGAND-BASED APPROACHES**

Drug design based on Ligand (or indirect drug design) relies on knowledge of the other molecules that bind to the biological target of interest. The general ligand-based VS methods are pharmacophore modeling, accordingly analysis, and QSARs.

**LIGAND-BASED PHARMACOPHORE MODELING**

A pharmacophore describes the 3D arrangement of steric and electronic features that are necessary to trigger or block a biological response, according to the definition of Wermuth et al [Lindberg etal., 1998]. Ligand-based pharmacophore model generation depends on the information regarding the known biological activity without any structural information for the macromolecular target. Where all compounds share a chemical functionality there are few pharmacophoric features is placed. In scaffold hopping, the computational models that constitute the pharmacophores have shown unique potential [Lewis et al., 2010]. A diversity of pharmacophore modeling approaches has been developed, such as catalyst/discovery studio, phase [Dixon et al., 2006], MOE, and ligand Scout [Wolber et al., 2005].

**SIMILARITY ANALYSIS**

To compare a biological active inquiry molecule with a database molecule between the electrostatic /similarity analysis and fingerprint similarity analysis. 2D fingerprints are portion strings that encode the presence or absence of chemical substructures [Gillet et al., 2003]. With the fingerprint of a database molecule, the fingerprint of query molecules is compared for the similarity search. Approved 2D fingerprint algorithms include MDL's Molecular ACCess System (MACCS), Daylight fingerprints and Molprint2D, Scitegic's Extended Connectivity Fingerprints (ECFps) [Willett et al., 2006].

The most favorable algorithms for 3D shape-based similarity searches is Open eye ROCS. Database molecules aligned through ROCS are re-scored by the EON algorithm between the query and database molecules which determines the electrostatic similarity [Sherman et al., 2010].

**QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS**

The mathematical relationships between the structural attributes and the target properties of a set of chemicals QSAR describe. ADMET properties of database molecules with close chemical structures or QSARs are applied to predict the biological activities [Perkins and Fang et al., 2003]. The multitude different of 1D, 2D, 3D, and multidimensional QSAR approaches has been progressing during the past several decades [Khedkar et al., 2010]. QSAR models are regularly created using a training set of different ligands, and the models are afterward tested against the test set of ligands Fischer and Lill et al., 2007].

**STRUCTURE-BASED APPROACH**

The 3D structure of pharmacological target protein is based on structure-based VS techniques that can be applied for a drug design. The ligand-based VS are more shown expensive due to structure-based methods [Waszkowycz et al., 2008]. This is a unique type of protein-ligand interaction which leads to optimization of the valuable tools.

**HOMOLOGY MODELLING**

The large gap between the number of experimentally solved protein structures and the number of available sequences which have been limited by the time, cost, and experimental challenges intrinsic to the process of structural determination, which have been operated homology modeling resolved can be possible. The homology modeling plays an important role in the structure-based drug discovery process in the absence of experimental structures. Homology or comparative modeling is a process, which is predicting protein structure from the universal observation that proteins with similar sequences have a similar structure. A few popular docking software programs are AutoDock, FlexX, DOCK, GOLD, MOEDock, eHiTs, Surflex, and Glide [Eswar and Cavasotto et al., 2009].

**PROTEIN-LIGAND DOCKING**

The protein ligands are used to confirm and orientation within their binding site and attempt to place the ligand into their appropriate interacting with the receptor [Bajorath etal., 2006]. The protein-ligand is used for docking which process is divided into two categories: the estimation of ligand affinity using a scoring function and the correct placement of the ligand at the protein binding site. They also stimulate the molecular dynamics and genetic algorithms to "evolve" new low energy conformations [Dias et al., 2008 and Huang et al., 2010]. However, their compounds have binding affinities, which is challenging [ Warren et al., 2006].

**MOLECULAR DYNAMICS SIMULATIONS**

The molecular dynamics simulations have become progressively useful in studying biological systems applicable to drug discovery[Salsbury et al., 2010 and

Wenzel et al., 2011]. The experimentally obtained protein structure is not suitable for structure-based VS. In some cases, for example, the structure represents a closed conformation of a protein which is the motion of a hinge region blocks to approach the ligand-binding pocket [Marco et al., 2007]. To determining the open conformation of proteins, the co-factor binding is predicted through MD simulations by induced conformations along with the structure-based VS. To understanding the feature is important for ligand-binding affinity, MD simulations play a significant role [Amaro et al., 2010].

**STRUCTURE-BASED PHARMACOPHORE MODELLING**

In the spatial information regarding the target, protein creates a topological description of ligand-receptor interactions in which the structure-based pharmacophore modeling is used. From the starting of 3D coordinates of a ligand bound to a macromolecular target, between the two binding partners the possible interactions are assessed. To ensure authenticity, it is essential for the binding-site residues and ligand coordinates due to the visual inspecting their degree of capability to the corresponding density map available, for instance, at the Uppsala Electron Density Server [Harris et al., 2004]. Based on the opposing chemical functionalities and the geometric arrangement about each other, where the interactions are observed, there are the pharmacophore features placed on the ligand side.

**CONCLUSION**

Several traditional plants are used to treat antidiabetic, hypoglycemic, and antihyperglycemic activities, and α-glucosidase and α-amylase inhibition has been reported. The antidiabetic effect of plants is a mixture of phytochemicals or single components of the plant extracts. The beneficial effects of phytochemicals, like regulation of glucose and lipid metabolism, stimulating β cells, insulin secretion, inhibition of gluconeogenic enzymes, Nf-kb signaling pathway, and rose protective action. Therefore, different types of medicinal plants may be useful to the fordesigning of new functional foods with antidiabetic properties.

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**Conflict of Interest :**

The authors declare that there is no conflict of interest.

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